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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/240,410	01/29/99	MICHALOVICH D	GP-30039

HM12/0510

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EXAMINER	
GRASER, J	
ART UNIT	**PAPER NUMBER**
1641	16

DATE MAILED: 05/10/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/240,410	Michalovich et al.
Examiner	**Group Art Unit**
Graser, Jennifer	1641

☒ Responsive to communication(s) filed on *Request for CPA , IDS # 14 & Prel. Amdt. B* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits** is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *2, 6-8, 10, 11, and 13-19* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) *6-8, 10, 11, 13-16, 18, and 19* is/are allowed.

☒ Claim(s) *2 and 17* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *14*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Continued Prosecution Application

1. The request filed on April 19, 2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/240,410 is acceptable and a CPA has been established. An action on the CPA follows. Acknowledgment and entry of the Amendment submitted 5/4/00, Paper No. 15B is made. Claims 2, 6-8, 10, 11 and 13-19 are currently pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Allowable Subject Matter

2. Claims 6-8, 10, 11, 13, 14, 15, 16, 18 and 19 are allowed.

Claim Rejections - 35 USC § 112

3. Claims 2 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for polynucleotides which comprise a polynucleotide sequence that has "at least 95% identity to a nucleotide sequence which encodes a polypeptide comprising the amino acid of SEQ ID NO:2, wherein said polynucleotide sequence may include up to n_n alterations..." (as recited in claim 2). This claim language allows for 93 nucleotide alterations to the degenerate sequences. However, the specification provides no guidance as to

what nucleotides may be changed without causing a detrimental effect to the protein to be produced. Further, it is unpredictable as to which nucleotides could be removed and which could be added. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of success are limited. Other positions are critical to the protein's structure/function relationship, e.g., such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spacial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions. To start with the DNA sequence first, this requires even more work on the part of the skilled artisan. Applicants have provide no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made. Given the lack of guidance contained in the specification and the unpredictability for determining acceptable nucleotide substitutions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

The specification is not enabled for polynucleotides which comprise a polynucleotide sequence that has "at least 95% identity to that of SEQ ID NO:1, wherein said polynucleotide sequence may include up to n_n nucleotide alteration over the entire length of SEQ ID NO:1..." (as recited in claim 17). This claim allows for numerous nucleotide alterations to the nucleotide sequence. However, the specification provides no guidance as to what nucleotides may be changed without causing a detrimental effect to the protein to be produced. Further, it is

unpredictable as to which nucleotides could be removed and which could be added. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of success are limited. Other positions are critical to the protein's structure/function relationship, e.g., such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spacial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions. Applicants have provide no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made. Given the lack of guidance contained in the specification and the unpredictability for determining acceptable nucleotide substitutions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Response to Applicants' Arguments:

Applicants argue that claims 2 and 17 do not contain a limitation that the claimed polynucleotides produce a polypeptide. Applicants state that the claims are directed to isolated polynucleotides comprising a nucleotide sequence that is at least 95% identical to a sequence that encodes SEQ ID NO:2 and the nucleotide of SEQ ID NO:1, respectively. This argument has been fully and carefully considered but is not deemed persuasive in overcoming the rejection. Claim 2 is not just drawn to a polynucleotide sequence which is at least 95% identical to a sequence which encodes SEQ ID NO:2, the claim language allows for 93 nucleotide alterations to

the degenerate sequences. It is not clear what purpose this sequence would serve as it would not necessarily produce a protein, nor possess the ability to be used in detection assays due to the numerous alterations allowed. Further, the specification has not specifically taught these sequences. The claims are much broader than what is taught by the instant specification, see written description rejection below. Applicants argument that the specification provides serveral uses for these claimed polynucleotides has been fully and carefully considered but is not deemed persuasive in overcoming the invention because the specification does not teach any of the particularly claimed sequences or their successful use in any of these uses.

Claim Rejections - 35 USC § 112-written description rejection

4. Claims 2 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth SEQ ID NO:1 and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to polynucleotides which comprise a polynucleotide sequence that has "at least 95% identity to a nucleotide sequence which encodes a polypeptide comprising the amino acid of SEQ ID NO:2, wherein said polynucleotide sequence may include up to n_n alterations..." (as recited in claim 2) or polynucleotides which comprise a polynucleotide sequence that has "at least 95% identity to that of SEQ ID NO:1, wherein said polynucleotide

sequence may include up to n_n nucleotide alteration over the entire length of SEQ ID NO:1..." (as recited in claim 17).

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself

is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

No disclosure, beyond the mere mention of allelic variants is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guildlines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated DNA molecule comprising a DNA sequence consisting of nucleotides SEQ ID NO:1 and equivalent degenerative codon sequences thereof, but not the full breadth of the claims meets the written description provisin of 35 USC 112, first paragraph.

5. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette,

1096 OG 30 (November 15,1989). The Group 1641 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jennifer Graser
JENNIFER GRASER
PATENT EXAMINER
5/8/00